TOBACCO INDUSTRY RESEARCH COMMITTEE

350 Fifth Avenue New York 1, N. Y.

Application for Research Grant

Date: December 15, 1954
(Revised copy)

1. Name of Investigator: William S. Murray, Sc.D.

2. Title: Research Associate and Administrative Director

3. Institution & Address: Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.

4. Project or Subject: The production of genetically controlled animals and tumors for possible use by T.I.R.C. grantees in experimental research on tobacco in relation to health by (a) the expansion of known inbred stocks and sources of tumor supply; (b) the production of such hybrids of heterozygous types as become necessary; and (c) the relation of this material to specific experimental work at the Laboratory.

5. Detailed Plan of Procedure: The use of genetically controlled strains of animals has become an accepted principle in medical research. The employment of such controlled animal material in research projects to be initiated by, or supported by the Tobacco Industry Research Committee has been approved as a policy by its Scientific Advisory Committee.

As a corollary of this policy, it is recognized that, if genetically "mixed" animals are to be used for some particular purpose, it will be much more satisfactory and much more adaptable to critical analysis if these heterogenous mixtures are produced in a repeatable manner by the interbreeding of known stocks.

The Jackson Laboratory has the most extensive, diversified, and complete representation of inbred mice available to medical researchers. It is therefore in a unique position to undertake the extension of existing strains, the development of new strains, or the producing of desired combinations of inter-strain hybrids. This statement applies also to the many types of tumors produced and maintained by transplantation.

Mice raised at the Jackson Memorial Laboratory have the following advantages over commercially produced animals:

1. They are obtained by expansions from carefully controlled nucleus stocks;

2. They are systematically checked for purity of strain and indications of infection;

3. They are carefully graded as to sex, age and weight;

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4. The Colonies are supervised by trained geneticists, who have the cumulative knowledge and experience of some 20 resident scientists, trained also in other disciplines, readily available for consultation. The value of supervision and study by the Laboratory Staff is apt to be underestimated. It will be recalled that statements have been made to the effect that cigarette smoking increases the probability of cancer in general. The constant investigation of the large genetically controlled colony of mice at Bar Harbor is providing increased knowledge of the etiological factors characteristic of many types of cancer. This will allow an increasingly accurate estimate of the independence and interrelationships of various sorts of neoplasms. While the degree to which such work applies to humans will remain debatable, the fact remains that relationships and principles discovered will continue to be of significance as have all phases of comparative medical research.

5. The genetic qualities of the inbred strains; their incidences of malignancies of various types; their morphological and physiological characteristics are supported by a 30 year accumulation of data. This accumulation of information is perhaps the greatest value of these animals, in that it enables the Staff to advise scientists who are about to undertake specific problems on the selection of the animal material best adapted to provide a critical assay of their research.

   Some idea as to the extent of this material may be given as follows. There are some sixty (60) strains of mice which are being maintained at the laboratory. These differ in the indicence of adenocarcinoma of the lung from 85 ± % in the highest strains to 0.1% in the lowest. Lung tumors may be isolated as the only type of neoplasm in some strains and occur in conjunction with other neoplasms in others. Data are being collected continuously on the "natural" incidence of lung tumors in these strains. Such data would be significantly augmented by the proposed grant.

   Additional animals produced and observed will also increase the incidence of new mutations and substrains, at least some of which should be useful in research of interest to the Tobacco Industry Research Committee.

At the present time the Laboratory is raising a total of 1,100,000 mice per year. Of these, 700,000 are used in the problems of its own staff and for the replenishment of the breeding colonies of the 60 inbred strains maintained and for carrying on 26 transplanted tumors. The remainder are observed and studied for genetic variations and are then sold to some 400 laboratories and hospitals in 43 states and the District of Columbia. Smaller numbers are shipped to laboratories in 22 foreign countries, covering every continent.

During the last five years, the Laboratory has been faced with an ever increasing demand for its excess animals. Requests for almost twice the number of animals the Laboratory is now able to produce are continuously on file.

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Source: https://www.industrydocuments.ucsf.edu/docs/qjvm0000

In the Laboratory's own research there are many problems which will be directly or indirectly aided by the proposed grant. A number of these may lead to prospects which will later be submitted individually to the Tobacco Industry Research Committee by the investigator or investigators concerned. As examples may be cited work by Dr. Kaliss on the effect of stress on tumor incidence in mice; the experiments on stress in relation to behavior, nervous stability and memory in dogs by Drs. Fuller et al; work on the influence of various carcinogens on transplants of cancer susceptible and non-susceptible lung tissue of mice by Little et al; and the approach to the successful synthesis of artificial culture media for animal tissues (Waymouth et al).

Profision of facilities and personnel for the purpose of producing additional animals is an imperative need.

It is requested that the Tobacco Industry Research Committee consider a grant in support of the effort to meet this need, on the understanding that research projects supported by the T.I.R.C. will receive first consideration in the sale of the increased number of animals which will be made available.

6. Budget Plan:

For the first year, 1955-56

| | |
|---|---|
| Salaries | $ 20,554.00* |
| Expendable Supplies | 7,585.00 |
| (1)Permanent Equipment | 9,350.00 |
| (2)Overhead (at 15%) | 5,623.00 |
| Other | - |
| (Total) | $ 43,112.00 |

For Succeeding years

| | |
|---|---|
| ~~Salaries~~ | ~~20,554.00~~ |
| Salaries | 20, 554.00* |
| Expendable Supplies | 7,585.00 |
| (3)Overhead | 4,220.00 |
| | $ 32,359.00 |

*This does not include salary of Principal Investigator.

(1) This involves racks for cages and the necessary alterations of space for the work.

(2) This item has been reduced to conform with the general policy of the Scientific Advisory Board.

(3) This item is smaller than in 1955-56 because of non-recurrence of the "Permanent equipment" item.

The grant requested will by no means cover the whole cost of scientific personnel needed to supervise and check the genetic qualities of the animals studied, or of the overhead needed to provide the facilities for their production. It will, however, justify the Laboratory in undertaking the production of a significant number of additional animals for the purposes mentioned. It will also make an important contribution to further and more complete genetic analysis of the various inbred strains, and their hybrids, and of the tumors which they produce both naturally and by induction. This will make the material studied increasingly valuable for all types of medical research.

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7. Anticipated Duration of Work: This is a continuing problem of parallel duration with the interest of the Tobacco Industry Research Committee in any phase of experimental research on tobacco in relation to health which includes the use of controlled animal material to be used in vivo or ~~in~~ in vitro.

8. Facilities and Staff Available: The proposed plan will not require the acquision of additional professional personnel. The Laboratory is at the moment constructing quarters for the proposed expansion and plans to staff these new quarters with caretakers and research assistants now in training. These will be augmented by new personnel in the unskilled categories.

The facilities, equipment and services of the Laboratory plant, valued at $1,164,000.00, will be available to this effort. The present mechanized cleaning and sterilizing equipment has capacity for the proposed additional load.

9. Additional Requirements: None.

10. Additional Information: On the basis of past performance, this plan should make available, to research outside the Laboratory, an additional 100,000 mice per year.

Signature /s./ William S. Murray

Director of Project

/s./ Dale J. Foley

Business Officer of the Institution

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